THE PROBLEM OF UTERINE CANCER.*

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During the last few years, there has been attracted to the Woman's Clinic of the University of California Hospital—in large part because of our work with radium—an ever increasing number of cases of uterine cancer. No one, I am certain, could study the data offered by this mass of material without concluding very definitely that the general profession is doing little to improve the cancer situation, and that this disease in the hands of men doing surgery is quite as hopeless as it was years ago when MacMonagle reported his series of 481 hysterectomies for uterine cancer with only two ultimate cures, and when Baldy confessed that he had never cured a case by any form of treatment.

There is no doubt but that we may not attain a proper solution of the cancer problem until the laity is educated to appreciate the importance of the earliest symptoms. Yet such education will avail but little a patient who falls into the hands of one who has not yet recognized the essentials of proper treatment. I, for one, believe that we will make greater headway in our problem by devoting our chief effort at present to the physician rather than to the laymen, since the physician has long been led afield by a mass of conflicting literature.

To my mind, a large part of the confusion in the literature has developed because the earlier student of cancer grouped in his investigation cancers from all parts of the body, ignorant of the fact that cancers differ markedly among themselves. In the same manner, our gynecologic literature teems with contradictory statements because so many have grouped together in their study all uterine cancers, which differ so markedly among themselves in habits of growth. Cancer of the cervix constitutes the problem of uterine cancer because so few are cured. In comparison with cervical cancers, the carcinomata of the uterine body lose their importance since they usually permit of cure.

Leucorrhea and haemorrhage are the only symptoms of operable cervical cancer. Yet we are constantly disappointed in finding that many cases are frankly inoperable even though they present for treatment shortly after the first sign of bleeding. There is, however, a clear reason for this fact. Only about one tenth of the cervical cancers are everting in type, and thus capable of giving early symptoms from bruising of the growth. In the other nine tenths, the growth early inverts or infiltrates and thus has but little chance to bleed until it has extended sufficiently far out to permit of slough of the older areas which have been deprived of necessary circulation. Moreover, with the advent of the first haemorrhage, the case is complicated by the presence of an infected ulcer. We can clearly see that if we await the development of bleeding that we may not hope to cure in the mass of cervical cancers. Hope lies only in the recognition of leucorrhea as the only safe early sign, and prophylactically, in the early repair of cervical lacerations and the proper treatment of gynecologic disease, since cancer is practically unknown in women who have not borne children or who have not had some pelvic disorder.

There is no doubt that we will make a long step forward when all students are taught to clearly differentiate the symptoms of inoperable and operable cancers. We, as physicians, chiefly interested in cure, are concerned primarily with cancer in an operative stage, since there is no doubt but that at the present time surgery offers the only chance of cure. Why, then, should we present without proper emphasis, in surgical treatises, cachexia and other late symptoms which are not symptoms of operable growths.

Yet we may not hope to combat successfully this disease which kills annually in the United States more than 11,000 women, without universal and long continued education. In the long intervals until the arrival of that era, we will be concerned with the treatment of all cases in all stages of growth, just as now, and the cure of cancer presents many problems. We, as surgeons, do not always recognize the features peculiar to cervical cancer. In marked contrast to the malignant tumors of the breast, ulceration is the almost universal rule. And the ulcer, moreover, is responsible for a large part of the symptomatology and many of the findings. From the walls of the ulcer comes the bleeding. The pelvic glands enlarge from absorption from the infected area. The parametria infiltrates from extension of the infection. In the breast enlarged axillary glands mean cancerous involvement since cancerous ulcers of the breast are comparatively rare. On the contrary, the pelvic glands first swell from absorption from the ulcer. While they may contain cancer cells, yet seldom save in late cases is the enlargement due to them. The treatment of the ulcer is a most vital thing and we must not lose sight of its importance.

Radical removal, although impeded by the presence of the bladder, ureters and rectum and an infected field, is strictly possible in selected cases. Cases are cured, yet its percentage in this country is not nearly as large as many would induce us to believe. We, therefore, must plan to operate properly the greatest number, since all cases not treated by proper operation will surely die. Long before Halsted evolved the modern operation for cancer of the breast, there were radical operations for uterine cancer. With this in mind, is it not of interest that it has remained for the breast surgeon to prove without doubt that you may not safely incise cancerous tissue and delay operation? Yet men who would not dream of thus attacking suspicious areas in the breast, daily remove tissue from the cervix and await for a long time a pathological report, apparently ignorant of the fact that by so doing, the patient loses her chance of cure. The same holds true for curettage to clean up the infected ulcer. It is high time that all

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surgeons learn that the excision of cancerous tissue must be followed by an immediate radical operation.

Many have offered in defense of such error that the early diagnosis may be a difficult thing, to be decided frequently only by an expert pathologist, so that there may be reason for such delay. Yet this does not hold. Cancer operations are not emergencies and the needed consultation can be easily arranged. Moreover, the public will soon learn that a man who is not a pathologist is not a safe person to be entrusted with such a formidable operation as the radical removal of a cancerous uterus. The pathologist also will learn that the older and slower methods of fixing tissues for microscopic study while suitable for post mortems have no place in an operating room. Surgical pathology demands immediate diagnosis, which constitutes no problem, since it deals with living cells which permit of frozen sections and the staining of living tissues.

Yet the removal of tissue prior to operation, objectionable as it is, does far less harm than the simple hysterectomy designed as cure. I am perfectly aware that the literature of the past supports the performance of such operations based often upon the statement that the growth is limited to the uterus in 40% of operable cases, and that it invades only by direct extension, a fallacy disproven long years ago by Ries, Kundrat, and Sampson and many others. Moreover, many who are fully aware that simple hysterectomy rarely if ever cures, still insist that it is useful as a palliative measure to check bleeding and to make the patient generally more comfortable. Personally, I have never seen a late case whose condition was improved by operation. More than twenty years ago, no less an authority than Sanger abandoned such treatment on the ground that the reverse was true, since it gave no hope of cure in extended growths and actually intensified the subsequent suffering. Case after case comes to our clinic for radium with infected ulcers and large pelvic masses almost fresh from the hands of surgeons who have done the simple hysterectomy, proving the long established rule that it is worse than useless to cut through cancerous tissues. We have learned also by experience that radium does not do much for the improvement of such cases.

Out of the myriads of cancer articles has come the now accepted truth that we are justified in surgical measures only when they are most extensive, and that all operations should be restricted to early cases. The large remainder are better treated by radium. Experience is teaching us daily that if there is question as to operability, the case does not permit of cure by surgery. Education of the laity and physician alone will bring us earlier cases, since the extreme of operative treatment has been reached in the extended operation.

The truly radical removal is a formidable operation, not only with a fixed primary mortality but with much morbidity as well, yet its basis is firmly proven by hosts of investigators. Considerable work has been done in this country. The most interesting of this was done by Sampson who, in 1906, reported the study of 27 specimens removed by his most extensive operation. Like Kundrat, he made complete serial sections, a tremendous yet necessary labor. He demonstrated by this means that a parametrium may be indurated without cancerous invasion; that it may present as normal and yet contain cancer; that soft and normal feeling glands may present cancer cells even though the parametrium is free from them; that the parametrium was cancerous in 62% of his cases; and that the lymph nodes in the pelvis were involved in nearly one-half of his operable cases. The operation of Ries, then, alone is perfect in theory since it removes the glands as the primary step of of the operation, a method most necessary since we may recognize cancerous glands only by microscopic serial sections. Moreover, late recurrences after a truly extended operation are regional rather than local, since they are from cancer in glands which have escaped removal, because carcinoma cannot arise from glands, since they do not contain epithelium.

Yet few hold that this perfectly designed operation is the one of choice because of the undecided question as to whether the increased primary mortality from such formidable surgery will more than offset the ultimate cure in a group of women who are late in life. But Ries' contention is worth considering. At the discussion of Wertheim's paper at the Chicago Gynecological Meeting in 1907, Ries again called attention to the fact that cancer ultimately and invariably kills unless removed; that the primary mortality of a truly radical operation is fixed relatively and that great reductions from it mean more often restriction of the extent of removal than perfection of the operator's technique. Yet the operation of Werder of Pittsburgh, popularized by Wertheim, represents the extreme of radical operations for which we now all plead adoption. It calls for the removal of the uterus, tubes and ovaries, one half the vagina and the parametria as far out as the pelvic walls in one piece after isolation of the ureters. Less than this should not be done on cervical cancers which come to operation. Yet many do a makeshift operation, free the ureters but leave their bed, removing little more than the ordinary hysterectomy, saving the operator much chance of a primary death but dooming the patient to ultimate death from cancer.

I agree with Peterson that a surgeon may have a right to dodge the issue and save a primary death under certain circumstances, if one does not include such cases in the list of extensive operations, since they give otherwise a false conception of the primary mortality. Nor is it necessary to state in our cancer series what cases were operated radically unless controlled by the ultimate results. The number of cases that survive five years or more alone determines what cases were treated radically.

Experience with radium convinces me that early growths are best treated by extended removal, and all others by radium, which has no equal as a

palliative measure. Whether radium cures or not may be an open question, but nothing treats so successfully a case which does not permit of extensive operation. It is more than likely, however, that early cases alone permit of cure, be the treatment what it may. A year ago, I reported my work with 50 to 90 mgs. of radium. We now believe that these amounts are small if one seeks a cure. We are now working with 100 and 150 mgs. The point is often advanced that radium treatments should precede all operations. A year ago, I reported a case operated after radium presenting many pelvic adhesions. We have had very recently one other case of operation after a seemingly inoperable growth had been made apparently operable by radium treatments. Under its use the ulcer disappeared and the vaginal vault became smooth. The parametria became softened and the uterus felt free. Yet a removal proved impossible since the growth extended far out beyond the ureter which was imbedded in a mass of softened cancerous tissue, adding one more proof that we should select our cases either for extensive operation or radium alone.

Finally, we present these points as conclusions:

I. Early cases alone afford hope of cure and the education of physician and laity is necessary before results show marked improvement.

II. Pre-operative removal of tissue for microscopic study must be followed by immediate operation if operation is contemplated.

III. The presence of an ulcer complicates the problem of uterine cancer.

IV. The curette should not be used in cleaning up an ulcer.

V. Early cases alone should be operated and only by the extended operation.

VI. All other cases should be treated by radium.

VII. Simple hysterectomy has no place whatever in the therapeusis of cervical cancer.

REFINEMENT OF COLORIMETRIC METHODS WITH SPECIAL REFERENCE TO INDIGO CARMINE AS A FUNCTIONAL TEST.*

(A Preliminary Report.)

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Accepted as probably the most valuable single test of Renal function. Phenolsulphonephthalein as proposed by Rountree and Geraghty (1) has won the deservedly high place it holds. With others we have found it to have every particle of value claimed for it, nor is it any part of our purpose to detract from its worth. Phthalein does, however, have the misfortune to be unserviceable in the presence of hematuria. This shortcoming is not due to any weakness of the dye as a test, but is inherent in the limitations of colorimetric methods. Color tests being dependent upon percentage comparison against a standard, phthalein can not be so compared when contaminated with hemaglobin, for the standard is red and the urine to be compared is brown.

This is particularly unfortunate in prostatic hypertrophy for, though we may gain valuable information of waste retention through the use of blood chemistry, and even more from blood cryoscopy, (now falling into disuse because of the technical skill and time required for its performance) we are still left much in the dark regarding excretion, when the Phthalein test becomes unavailable.

In the futile effort to make Phthalein tests under these conditions,—i. e., when contaminated with blood,—and finding that we were actually not making color. comparisons at all, but were merely matching densities with fair success, our attention was attracted to the fact that we were doing practically the same thing in amber colored urines. We were at this time using the Helleger colorimeter, and our suspicion having been aroused by the inability to compare reds with various shades of red-brown, we determined to investigate the matter thoroughly. We tried the makeshift of interposing various shades of amber glass between the light and the standard, but with small satisfaction. The Helleger colorimeter, being rapid and simple, and being perhaps in more common use than any other except the Dunning, we felt that whatever difficulties we were having others were having also.

For a long time also we had felt dissatisfied with the comparatively low Phthalein values secured from cases investigated in routine work where no kidney involvement was thought to be present. The question was raised in our minds as to why our normals would not agree with the normals found by the originators of the test. In referring to the original article we found that the Dubosq colorimeter, an instrument not easily obtainable, had been used.

Geraghty (2) says of the wedge-shaped Helleger colorimeter that it is "approximate." If a test is to be really of value it must be correct, not approximately correct, for if not how is one investigator to compare his findings with those of another, and how is he to reconcile them with the carefully tabulated series of cases presented by the originator of the test! This applies to all tests, if they are to be of any scientific value whatever.

Geraghty, among his seven postulates of the ideal functional test, asserts (2): "It should afford an indication of the absolute work accomplished as well as the relation of this to the normal standard under all conditions." Any technique giving only approximately correct readings does not fulfil this condition. It therefore became our desire to find out, if possible, how far from correct were the readings of the two colorimeters in most common use, and to discover some simple method of correction.

Fortunately for our purpose at about this time a new and very simple colorimeter was proposed by Peebles. (3) The principle is that of com-

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